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Introductory Remarks to the Third Session

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Introductory remarks to the third session

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This session is of particular personal interest to me. Almost exactly four years ago I completed the manuscript of my book with a section on glycolytic enzymes. At that time, some very interesting and tantalizing results were emerging from the crystallographic laboratories in Bristol and Oxford, so I paid visits to Dr Watson and Dr Muirhead and Professor Phillips with the result that I was able to include some speculative, unpublished, ideas on mechanism. It is now most intriguing to see the progress since 1976 and how some early speculations have held up or developed.

The first speakers in this session, Dr Watson and Dr Fothergill, had just found a most striking feature at the active site of phosphoglycerate mutase: the two imidazole rings of the active site histidines are parallel and only 4 Å apart, apparently well set up for shuffling the phosphate between 2-phosphoglycerate and 3-phosphoglycerate via two phosphoenzyme intermediates. I see from the abstract that subsequent data conflict with this idea.

Dr Muirhead, the third speaker, had then the 3.5 Å resolution map of glucose-6-phosphate isomerase but no sequence data. On the basis of some inhibitor binding studies, she and Dr Shaw proposed a novel and elegant chemical mechanism and some reinterpretation of existing data on chemical modification. I ended up the section in my book on this enzyme with the one-sentence paragraph: 'It will be interesting to see, when the enzyme has been sequenced, whether or not the crystallographers guessed correctly about the amino acid side chains.' I see from the abstract of Dr Muirhead's paper that some sequence is now available.

At Oxford, Professor Phillips's group had just had the rare opportunity of solving the structure of a productive enzyme–substrate complex. This is possible for triose phosphate isomerase since it catalyses a simple equilibrium between one substrate and one product and the equilibrium constant favours one form, dihydroxyacetone phosphate. I see from the abstract that a detailed mechanism is now being proposed.

Also at that time I had the enjoyment of studying in depth the work of Dr Rose, who has been one of the most innovative enzymologists of the past twenty years. I look forward to hearing him and the other three speakers.